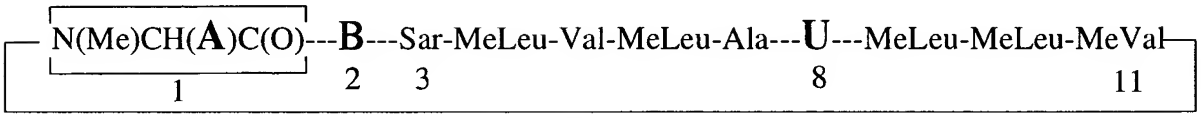
WHAT IS CLAIMED IS:

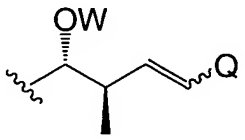
1. A cyclosporin analog of formula I or a pro-drug or a pharmaceutically acceptable salt thereof:



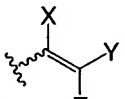
(I)

and

A is of the formula:



wherein:

Q is 

or 

, where

i) X is selected from hydrogen, halogen, C_1–C_6 alkyl, or aryl;

ii) one of Y and Z is selected from: hydrogen, deuterium, halogen, or methyl and the other is independently selected from:

a) halogen;

b) R_1, where R_1 is selected from:

1) hydrogen;

2) deuterium;

3) C_1–C_6 alkyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;

4) C_2–C_6 alkenyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;

5) C_2–C_6 alkynyl, optionally substituted with halogen, TMS, aryl, heterocycloalkyl, or heteroaryl;

6) C_3–C_{12} cycloalkyl;

7) substituted C_3–C_{12} cycloalkyl;

8) aryl;

9) substituted aryl;

10) heterocycloalkyl;

11) substituted heterocycloalkyl;

12) heteroaryl; or

13) substituted heteroaryl;

c) $-C(O)OR_1$, where R_1 is as previously defined;

d) $-C(O)OCH_2-V-R_1$, where R_1 is as previously defined and V is –O– or –S–;

e) $-C(O)N(R_3)(R_4)$, where R_3 and R_4 are independently selected from R_1 as previously defined;

f) $-C(O)SR_1$, where R_1 is as previously defined;

g) $-C(O)OCH_2OC(O)R_1$, where R_1 is as previously defined;

h) $-C(S)OR_1$, where R_1 is as previously defined;

i) $-C(S)SR_1$, where R_1 is as previously defined;

j) R_2, where R_2 is selected from:

1) C_1–C_6 alkyl–M–R_1, where R_1 is as previously defined and M is absent or selected from:

i. –NH–;

ii. $-N(CH_3)-$;

iii. –S–;

iv. $-S(O)_n-$, where n = 0, 1, or 2; or

v. –O–;

2) C_2–C_6 alkenyl–M–R_1, where R_1 and M are as previously defined; or

3) C_2–C_6 alkynyl–M–R_1, where R_1 and M are as previously defined;

k) Or in the alternative, Y and Z are taken together with the carbon atom to which they are attached to form a C_3–C_{12} cycloalkyl moiety; and

iii) G is independently selected from halogen, TMS, R_1 or R_2 as previously defined;

B is selected from:

i) –αAbu–;

ii) –Val–;

iii) –Thr–; or

iv) –Nva–;

U is selected from:

i) –(D)Ala–;

ii) –(D)Ser–;

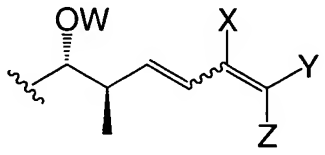
iii) –[O-(2-hydroxyethyl)(D)Ser]–;

iv) –[O-(acyl)(D)Ser]–; or

v) –[O-(2-acyloxyethyl)(D)Ser]–; and

W is selected from hydrogen or a hydroxy protecting group.

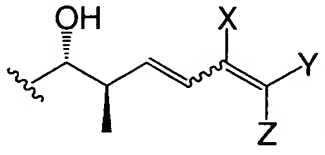
2. A compound formula I according to claim 1, wherein A is of the formula **A1**:



(A1)

where W, X, Y, and Z are as previously defined.

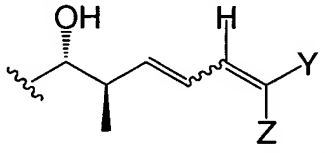
3. A compound of formula I according to claim 1, wherein A is of the formula **A2**:



(A2)

where X, Y, and Z are as previously defined.

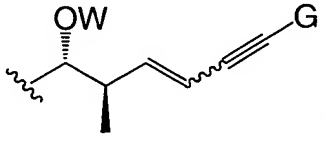
4. A compound of formula I according to claim 1, wherein A is of the formula **A3**:



(A3)

where Y and Z are as previously defined.

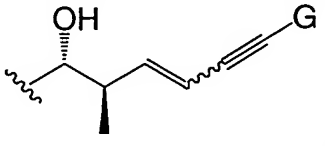
5. A compound of formula I according to claim 1, wherein A is of the formula **A4**:



(A4)

where W and G are as previously defined.

6. A compound of formula I according to claim 1, wherein A is of the formula **A5**:

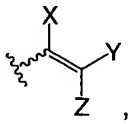


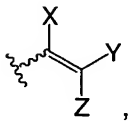
(A5)

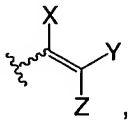
where G is as previously defined.

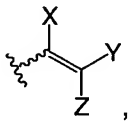
7. A compound of formula I, according to claim 1, selected from:

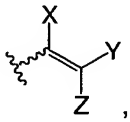
Example 1. A compound of formula I, wherin A is of the formula (**1**-2) and W is Ac;

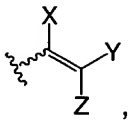
Example 2. A compound of formula I, wherein Q is  , W is Ac and X=Y=Z = hydrogen;

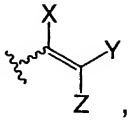
Example 3. A compound of formula I, wherein Q is  , W is H and X=Y=Z = hydrogen;

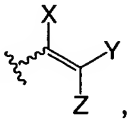
Example 4. A compound of formula I, wherein Q is  , Y is CH_3, and W=X=Z = hydrogen;

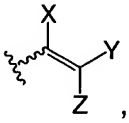
Example 5. A compound of formula I, wherein Q is  , Y= Z= CH_3, and W=X = hydrogen;

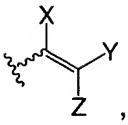
Example 6. A compound of formula I, wherein Q is  , Y is $-(CH_2)_3CH_3$, and W=X=Z = hydrogen;

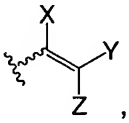
Example 7. A compound of formula I, wherein Q is  , Y is $-(CH_2)_2Br$, and W=X=Z = hydrogen;

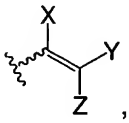
Example 8. A compound of formula I, wherein Q is  , Y is *ortho*-Me-phenyl, and W=X=Z = hydrogen;

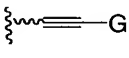
Example 9. A compound of formula I, wherein Q is  , Y is *ortho*-Br-phenyl, and W=X=Z = hydrogen;

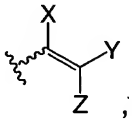
Example 10. A compound of formula I, wherein Q is  , Y is $-CO_2Me$, and W=X=Z = hydrogen;

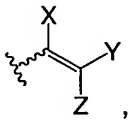
Example 11. A compound of formula I, wherein Q is  , Y is *meta*-CHO-phenyl, and W=X=Z = hydrogen;

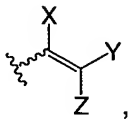
Example 12. A compound of formula I, wherein Q is  , Y is Et, and W=X=Z=hydrogen;

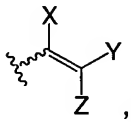
Example 13. A compound of formula I, wherein Q is  , Y is $-CH=CHCH_2TMS$, and W=X=Z=hydrogen;

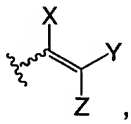
Example 14. A compound of formula I, wherein Q is  , G is H, and W is H;

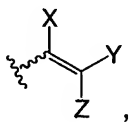
Example 15. A compound of formula I, wherein Q is  , Y is propyl, and W = X = Z = hydrogen;

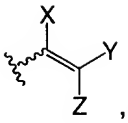
Example 16. A compound of formula I, wherein Q is  , Y is cyclopropyl, and W = X = Z = hydrogen;

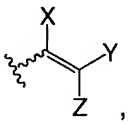
Example 17. A compound of formula I, wherein Q is  , Y is $-CH=CHCH_3$, and W = X = Z = hydrogen;

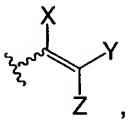
Example 18. A compound of formula I, wherein Q is  , X = Y = CH_3, and W = Z = hydrogen;

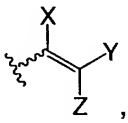
Example 19. A compound of formula I, wherein Q is  , W = X = Y = hydrogen, and Z = CH_3;

Example 20. A compound of formula I, wherein Q is  , Y is p-bromophenyl, and W = X = Z = hydrogen;

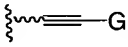
Example 21. A compound of formula I, wherein Q is  , W = X = Y = hydrogen, and Z = $-CH_2CH=CH_2$;

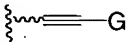
Example 22. A compound of formula I, wherein Q is  , W = X = Y = hydrogen, and Z is ethyl;

Example 23. A compound of formula I, wherein Q is  , W = X = Y = hydrogen, and Z = $-CH=CHCH_3$;

Example 24. A compound of formula I, wherein Q is  , W = X = Y = hydrogen, and Z = $-CH_2OCH_3$;

Example 25. A compound of formula I, wherein Q is  , G = $-CH=CHCH_3$ and W = hydrogen;

Example 26. A compound of formula I, wherein Q is  , G = propyl and W = hydrogen; or

Example 27. A compound of formula I, wherein Q is  , G = $-CH_3$ and W = hydrogen.

8. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of Formula (I) in claim 1, or a pharmaceutically acceptable salt, ester or prodrug thereof, in combination with a pharmaceutically acceptable carrier or excipient.

9. A method of treating organ transplantation rejection in a subject, which comprises administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 8.

10. A method of treating an immune disorder in a subject, which comprises administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 1.

11. The method of claim 10, wherein said immune disorder is selected from the group consisting of: rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, atopic dermatitis, allergic rhinitis, and chronic obstructive pulmonary disease.

12. A method of treating an immune disorder in a subject, which comprises topically administering to said subject a therapeutically effective amount of the pharmaceutical composition of claim 1.

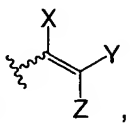
13. The method of claim 12, wherein said inflammatory or immune disorder is selected from the group consisting of psoriasis and eczema.

14. The method of claim 12, wherein said topically administering is achieved via inhalation.

15. The method of claim 14, wherein said inflammatory or immune disorder is an obstructive airways disease.

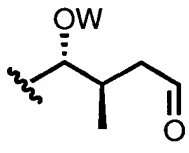
16. The method of claim 15, wherein said airways disease is selected from the group consisting of asthma, allergic rhinitis, bronchitis, cystic fibrosis, and chronic obstructive pulmonary disease.

17. The method of claim 16, wherein said chronic obstructive pulmonary disease is emphysema or chronic bronchitis.

18. A process for the preparation of a compound of formula I, wherein Q is 

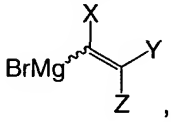
, wherein X, Y, and Z are as defined in claim 1, comprising

i) reacting cyclosporin A with a reagent capable of oxidative cleavage to form a compound of formula I, wherein A is represented by the formula:

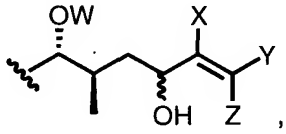


, where W is as defined in claim 1;

ii) reacting a compound formed in step i with a Grignard reagent of formula

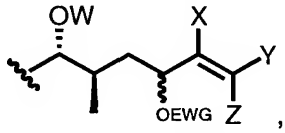


, where X, Y, and Z are as defined in claim 1 to form a compound of formula I, wherein A is represented by the formula:



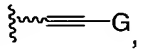
, wherein W, X, Y, and Z are as defined in claim 1;

iii) reacting a compound formed in step ii with an with an electrophile, such as, but not limited to, mesyl chloride, chloroformate, or triflate chloride to form a compound of formula I, wherein A is represented by the formula:



, wherein EWG is an electron withdrawing group and W, X, Y, and Z are as defined in claim 1; and

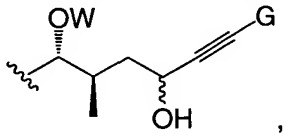
iv) reacting a compound formed in step iii with a palladium catalyst.

19. A process for the preparation of a compound of formula I, wherein Q is 

, comprising

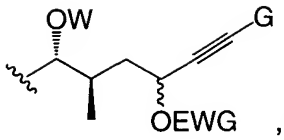
i) reacting a compound formed in step i of claim 18 with a lithium acetylide represented by the formula 

, wherein G is as defined in claim 1 to form a compound of formula, wherein A is represented by the formula



, wherein G and W are as defined in claim 1;

ii) reacting a compound formed in step i with an electrophile, such as, but not limited to, mesyl chloride, chloroformate, or triflate chloride to form a compound of formula I, wherein A is represented by the formula



, wherein EWG is an electron-withdrawing group, and G and W are as defined in claim 1, which then undergoes elimination.

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